Opinion

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The CRISPR babies controversy: Responsibility and regulation in the spotlight

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Plans and experiments to genetically modify human embryos using CRISPR-Cas9-based gene editing have triggered a substantial controversy within and beyond the scientific community. First concerns about the use of gene editing to modify the human germline were sparked by an experiment on non-viable human embryos on the β-globin gene [1]. In response, the first international summit on human gene editing was held in Washington, DC, in December 2015, which concluded in its final statement that "[i]t would be irresponsible to proceed with any clinical use of germline editing". By the end of 2015, CRISPR-edited babies were a technical possibility, but not reality.

Three years later, the situation had dramatically changed. On November 25, 2018, He Jiankui at the Southern University of Science and Technology in Shenzhen, China, announced the birth of twins who had undergone gene editing at the single-cell stage in order to prevent HIV infection. He's announcement came at the eve of the second international summit on human gene editing at the University of Hong Kong.

The response from the summit's organizing committee was that "the procedure was irresponsible and failed to conform with international norms" (final summit statement), and the experiment was criticized for its problematic study protocol, lack of transparency, and for being unethical. The chair of the summit commented that He's experiment represented a "failure of self-regulation by the scientific community". With He's announcement, human germline editing ceased to be an issue that could be dealt with by self-governance of the scientific community.

In addition to immediate responses at the summit, national committees, councils, and societies have issued similar statements, calling germline editing "irresponsible" and "a serious violation of ethical obligations" (German Ethics Council, 26/11/2018), "strongly condemn[ed] it for the extreme irresponsibility, both scientifically and ethically" (Genetics Society of China/Chinese Society for Stem Cell Research, 27/11/2018), that "a red line has been crossed" and that a "stronger global governance" was needed (French National Consultative Ethics Committee, 29/11/2018). The WHO, in December 2018, established an expert panel on the governance and oversight of human gene editing that has to date produced one comment, one statement, and two reports. It plans to publish its recommendations by the end of 2020, which will constitute the first global policy proposal in the domain.

In the media, the majority have taken a critical stance toward He's research, frequently calling it "irresponsible", "unethical", "illegal", and "dangerous" [2]. In comparison with the 2018 summit, they use similar arguments to condemn He—scientific, medical, legal, political, social, and moral ones—but also three additional ones: that He's experiment discredits China's reputation, that it is harmful to the public image of gene editing, and that it can have negative social consequences. One does find, nonetheless, positive remarks in social media and the press. There are numerous positive comments about He's video, with words like "breakthrough", "hero", "congratulations", "proud", and "brave", and there has been positive media coverage in the Ukraine and Russia.

In June 2019, Denis Rebrikov, a Russian biologist at the Pirogov Russian National Research Medical University in Moscow who also works at a fertility clinic, announced via a news article in *Nature* his plans to produce gene-edited babies [3]. Various scientists in the same article renounced his plans as "disappointing", "unsettling", "irresponsible", and "not [. . .] ethical". An accompanying *Nature* editorial argued that the "scientific community must intervene" [4] and calls for boycotts and moratoriums followed [5].

The WHO issued a statement that "advises regulatory or ethics authorities to refrain from issuing approvals concerning requests for clinical applications for work that involves human germline genome editing" and the Russian Ministry of Health released a statement that endorsed the position of the WHO, qualifying the use of gene editing on human embryos as "premature and irresponsible".

In the media, Rebrikov, like He Jiankui, was criticized on scientific, medical, legal, and ethical grounds. Russia's reputation was also discussed in several articles for "rattling the cage" of gene editing. But there are also positive comments. Many articles commented that Rebrikov is more "transparent" than He and that "[h]is openness to the subject is really a plus to shift the responsibility from a simple scientist or an institution to the shared responsibility where all of society is included" (quoted in [6]).

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There is an important difference though between He and Rebrikov: He announced his experiment post-factum after the births of the twins, whereas Rebrikov only revealed his plans to edit human embryos. The *Nature* editorial [4] argued that "[t]he scientific community now has an opportunity to [...] work with Rebrikov to identify and discuss the risks. That's better done by engaging with him than by branding him a maverick". Rebrikov has repeatedly stated that he will only move forward with producing gene-edited babies with a permission from the relevant authorities. The debate already had an effect: Rebrikov shifted his research focus from the CCR5 gene (the same gene that He Jiankui had altered) to the GJB2 gene (a gene that, when defect, can lead to congenital deafness) and changed his communication strategy—he now declines most interviews [6,7].

He Jiankui represents both the historical reference point and the worst-case scenario for human germline editing. He ended up being confined in several senses of the word: excommunicated by the scientific community, having his laboratory closed and his university contract terminated, and by being sent to prison for 3 years. While Rebrikov has not been fired nor physically detained, his work is criticized along the same lines as He's experiment, with the term "irresponsible" epitomizing the response from scientific institutions.

The CRISPR babies controversy will most likely have a rather chilling effect on public attitudes, values, and preferences concerning human gene editing. Research has shown that the public is often very interested in new technologies and how their use is linked to issues such as justice, trust, equity, and ethics. Engaging the public in the genome-editing debate—as the WHO, the UK Nuffield Council on Bioethics, and others have called for—is thus paramount to better understand the social, ethical, and legal ramifications.

I would like to conclude by outlining two possible future scenarios for inspiring further debate. In the first scenario, the search for a global and unequivocal response or consensus concerning human germline editing will prove pointless. As for climate change, it will not be possible to create a common international agenda, with concrete policies. Despite recommendations from international organizations such as the WHO, there will always be countries and scientists willing to move ahead or undermine collective standards and values.

In the second scenario, the debates sparked by He and Rebrikov will make the scientific community more reflexive and create spaces for analysis and debate, that eventually lead to more transnational, democratic, and robust governance. These will pave the way for a universally ratified treaty, comparable to the Montreal Protocol that led to the phasing out of ozone-depleting chlorofluorocarbons. The CRISPR babies controversy will be remembered as a particularly fertile episode, as it put human gene editing on both the political and the regulatory agenda with He and Rebrikov as "circumstantial whistleblowers".

References

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